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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,585	12/20/2001	Terry Roemer	10182-016-999	8340

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EXAMINER	
GUZO, DAVID	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,585	ROEMER ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-77* is/are pending in the application.

4a) Of the above claim(s) *1-31 and 43-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 December 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Applicant's election of Group XII, Claims 32-42, nucleic acid SEQ ID NO:6068 in the reply filed on 5/11/04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-31, 43-77 and SEQ ID NO:s 6001-6067 and 6069-6932 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Given the election of SEQ ID NO:6080, the corresponding primers 4048 and 5068 in Claim 36 will be examined and primers defined by SEQ ID NOs: 4001-4067, 4069-4932, 5001-5067 and 5069-5932 (in Claim 36) are withdrawn from further consideration. Election was made **without** traverse in the reply filed on 5/11/04. As noted in the restriction requirement, each SEQ ID NO (6001-6932) is not a separate species but a separate patentably distinct invention.

Applicants are required to amend the elected claims to eliminate reference to non-elected subject matter.

The Drawings are objected to. Figure 6 has letters, numbers and reference characters that are not at least .32 cm (1/8 inch) in height (See 37 CFR 1.84(p)(3)). Figures 1-2 contain numbers and reference characters which are not plain and visible in the shaded areas in the Figures. Objections to the Drawings will not be held in abeyance.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because it consists of TWO separate paragraphs. Correction is required. See MPEP § 608.01(b).

Priority for the claimed invention is granted back to the filing date of the instant application (12/20/01).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 34, 37, 39 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Kiebler et al.

Applicants claim a nucleic acid molecule comprising a fragment of one of SEQ ID NO.:6001 to 6932, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 and at least 100 consecutive nucleotides of SEQ ID NO: 6068 or a purified or isolated nucleic acid molecule obtained from an organism other than *Candida albicans* or *Saccharomyces cerevisiae* comprising a nucleotide sequence having at least 30% identity to SEQ ID NO: 6068, fragments comprising at least 25 consecutive nucleotides of SEQ ID N0:6068, the sequences complementary to SEQ ID NO:6068 and the sequences complementary to fragments comprising at least 25 consecutive nucleotides of SEQ ID N0:6068, as determined using BLASTN version 2.0 with the default parameters. Applicants also claim said sequences in a vector and a host cell containing said vector.

Kiebler et al. (Nature, Vol. 348, 1990, pp. 610-616, see whole article, particularly p. 614, right column and Fig. 5) recites a sequence from *Neurospora crassa* comprising a fragment comprising at least 10 nucleotides (see nucleotides 840-852 of the result 9 of the sequence search) of SEQ ID NO:6068 and comprises a nucleotide sequence having at least 30% identity to 25 consecutive nucleotides of SEQ ID NO:6068 (see nucleotides 695-719 of result 9 of the sequence search) wherein the percent identity is greater than 30% even if BLASTN version 2.0 with default parameters was used and a vector and host cell (λgt11 library in bacterial host cells) containing said sequence. Kiebler et al. therefore teaches the claimed invention.

To aid applicants in the sequence comparison, a printout of the sequence search result is attached.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 34, 35 and 39-42 are rejected under 35 U.S.C. 102(e) as being anticipated by Weinstock et al.

Applicants claim a nucleic acid molecule comprising a fragment of SEQ ID NO:6068, a nucleic acid molecule which hybridizes with SEQ ID NO:6068, a vector comprising a promoter operable in *C. albicans* or a regulatable promoter and a host cell containing said vector.

Weinstock et al. (U.S. Patent 6,747,137, issued 6/8/04, filed 2/12/99, see whole document, particularly SEQ ID NO:3520; paragraph bridging columns 14-15; column 15, lines 34-47; paragraph bridging columns 17-18; column 22; columns 24-25; column 44, lines 16-26) recites a sequence 99.3% identical to SEQ ID NO:6068 isolated from *C. albicans* as well as vectors containing said sequence wherein the sequence can be under control of a regulatable promoter or a natural *C. albicans* promoter and wherein the vector is in a host cell. Weinstock et al. therefore teaches the claimed invention.

To aid applicants in comparing the sequences, a printout of a sequence search is attached.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 34-35 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Applicants claim a nucleic acid molecule comprising a fragment of SEQ ID NO.:6068, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 and at least 100 consecutive nucleotides of SEQ ID NO: 6068 or a nucleic acid molecule comprising a nucleotide sequence that hybridizes under stringent condition to a second nucleic acid molecule consisting of (a) a nucleotide sequence selected from the group consisting of SEQ ID NO.: 6068, or (b) a nucleotide sequence that encodes a polypeptide consisting of SEQ ID NO.: 7068; wherein said stringent condition comprises hybridization to filter-bound DNA in 6x sodium chloride/sodium citrate (SSC) at about 45 C followed by one or more washes in 0.2xSSC/0.1% SDS at about 50-65 C. The nucleic acids are not recited as isolated or purified and hence read on products of nature. For example, claim 34 reads on a nucleic acid comprising a fragment of SEQ ID NO:6068 wherein said fragment can be the entire sequence of SEQ ID NO:6068 minus a single nucleotide mismatch (reading on naturally occurring single nucleotide polymorphisms) and claim 35 reads on SEQ ID NO:6068 since SEQ ID NO:6068 would hybridize under stringent conditions to the recited sequences. The claimed nucleic acids read on naturally occurring *C. albicans* nucleic acids molecules comprising the recited sequences.

Claims 32-42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility.

Applicants claim a nucleic acid sequence (SEQ ID NO:6068) which applicants claim as being essential for proliferation of *Candida albicans*, sequences comprising fragments of said nucleic acid sequence, sequences capable of hybridizing thereto, sequences having varying levels of sequence identity thereto, a vector comprising said nucleic acid sequence and a host cell containing said vector.

Applicants indicate, on pages 6-7 of the specification, that the claimed essential nucleic acid sequences can be used for several purposes:

> In a further embodiment of the present invention, a set of genes of a pathogenic organism are identified as potential targets for drug screening. Such genes comprise, genes that have been determined, using the methods and criteria disclosed herein, to be essential for survival of a pathogenic fungus and/or for the virulence and/or pathogenicity of the pathogenic fungus. The polynucleotides of the essential genes or virulence genes of a pathogenic organism (i.e., the target genes) provided by the present invention can be used by various drug discovery purposes. Without limitation, the polynucleotides can be used to express recombinant protein for characterization, screening or therapeutic use; as markers for host tissues in which the pathogenic organisms invade or reside (either permanently or at a particular stage of development or in a disease states); to compare with DNA sequences of other related or distant pathogenic organisms to identify potential orthologous essential or virulence genes; for selecting and making oligomers for attachment to a nucleic acid array for examination of expression patterns; to raise anti- protein antibodies using DNA immunization techniques; as an antigen to raise anti-DNA antibodies or elicit another immune response; and as a therapeutic agent (e.g., antisense). Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in assays to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The claimed invention is not supported by a specific, substantial or well established utility because none of the recited utilities for the claimed invention represents a utility that is well known, immediately apparent and in currently available

form. The basis underlying applicants' assertions for utility of SEQ ID NO:6068 is that it is an essential gene for *C. albicans* proliferation. The data for this assertion is based upon culturing the cells generated using GRACE methodology (one target allele is inactivated and the second is placed under a heterologous regulatable promoter) in a culture media *in vitro* under conditions where the second allele is not expressed and determining cell viability or growth. This method determines whether a given gene is essential for viability or growth **only under the specific culture conditions** applicants used to determine cell viability or growth, said gene may be non-essential under a different set of *in vitro* culture conditions (i.e. a different culture medium) or more importantly, under *in vivo* growth conditions. This is relevant to drug targeting studies because if SEQ ID NO:6068 is not essential *in vivo*, any drug identified would be of dubious use in treating a patient.

Applicants present no specific, substantial or well established utility for SEQ ID NO:6068, only the assertion that it, among hundreds of other genes, is an essential gene for proliferation of *C. albicans*. With regard to use of SEQ ID NO:6068 as a potential drug target, the nature of the target is critical in determining whether it can be a suitable drug target or not. Without a knowledge of the biological functions, structural and functional properties and expression profile of SEQ ID NO:6068 or the protein encoded by SEQ ID NO:6068, the skilled artisan would not be able intelligently screen drugs active against the gene or gene product. As noted by applicants on p. 34 of the specification:

Information regarding the structure and function of the gene product of the individual essential gene or virulence gene allows one to design reagents and assays to find compounds that interfere with its expression or function in the pathogenic organism. Indeed, without knowledge of the properties of SEQ ID NO:6068, it is unclear how one would interpret the effects of any given drug applied to cells comprising SEQ ID NO:6068, i.e. how would one ascertain, in a GRACE strain, whether any particular drug was acting on SEQ ID NO:6068 or the protein encoded by SEQ ID NO:6068 vs. some other non-target essential gene or gene product. The skilled artisan would need to conduct further research on SEQ ID NO:6068 in order to determine what it is in order to use it as a drug target.

With regard to assertions of utility of SEQ ID NO:6068 based upon characterization of the protein encoded by the sequence, use of said protein to raise antibodies, use of SEQ ID NO:6068 as a marker for tissues which the pathogen invades or resides in, use of SEQ ID NO:6068 to identify potential orthologous essential or virulence genes in other organisms, use of SEQ ID NO:6068 to select and make oligomers for attachment to a nucleic acid array for examination of expression patterns, use as an antigen for raising anti-DNA antibodies and as a therapeutic agent (e.g. antisense), it is noted that none of these utilities is specific and substantial for SEQ ID NO:6068. Utilities such as serving as a marker for tissues which the pathogen invades is not a specific utility because it applies generally to any nucleic acid contained in the pathogen (*C. albicans*) and is not specific to SEQ ID NO:6068. Use of SEQ ID NO:6068 to identify potential orthologous essential or virulence genes in other organisms is not a specific or substantial utility because applicants are using one

sequence with unknown function to identify other sequences with unknown function. It would require further research on the recited SEQ ID NO:6068 to identify its biological properties in order to begin to speculate upon the biological properties of any sequences homologous to SEQ ID NO:6068. Inclusion of SEQ ID NO:6068 or use of SEQ ID NO:6068 to make oligomers for attachment to a nucleic acid array for examination of expression patterns is not a patentable utility. Assuming *arguendo*, that a genetic gene expression assay – one based on monitoring expression of hundreds or thousands of uncharacterized nucleic acids would provide a useful tool for, e.g. drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has a patentable utility. Although each nucleic acid in an assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid – its data point – is only a tiny contribution to the overall picture. The *Brenner* Court held that 35 USC 101 sets more than a *de minimis* standard for utility. Providing a single data point among hundreds or thousands of others, even if the hundreds or thousands of data points collectively are useful, does not meet the standard of a utility which provides a specific benefit in currently available form. Utilities based upon further study of the nucleic acid in order to determine the function and properties of said claimed nucleic acid are not specific and substantial because they do not provide a specific benefit in currently available form.

Claims 32-42 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial asserted

utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34, 37-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim a nucleic acid molecule comprising a fragment of SEQ ID NO.:6068, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 and at least 100 consecutive nucleotides of SEQ ID NO: 6068 or a purified or isolated nucleic acid molecule obtained from an organism other than *Candida albicans* or *Saccharomyces cerevisiae* comprising a nucleotide sequence having at least 30% identity to a sequence from SEQ ID NO: 6068, fragments comprising at least 25 consecutive nucleotides of SEQ ID N0:6068, the sequences complementary to SEQ ID NO:6068 and the sequences complementary to fragments comprising at least 25 consecutive nucleotides of SEQ ID N0:6068, as determined using BLASTN version 2.0 with the default parameters. Claim 34 reads on a genus of nucleic acid sequences which comprise any allele or allelic variant of SEQ ID

NO:6068 as long as said allele or variant has a stretch of at least 10 or 20, etc. consecutive nucleotides of SEQ ID NO:6068. Claim 34 also reads on any fusion proteins having fragments of SEQ ID NO:6068. Claim 37 reads on potentially thousands of different undisclosed genes from the recited microorganisms or from any organism other than *C. albicans* or *Saccharomyces cerevisiae* wherein said genes have at least 30% identity to SEQ ID NO:6068 or fragments comprising at least 25 consecutive nucleotides of SEQ ID NO:6068, etc. as determined using BLASTN version 2.0 with the default parameters. Applicants disclose the single species SEQ ID NO:6068.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention. In the instant case, applicants present no disclosure of any nucleic acid sequences encoding any variants or alleles of SEQ ID NO:6068, no nucleic acid sequences encoding proteins, having the sequence relationships as recited in claim 37, from species such as *Aspergillus flavis*, *Botrytis cinerea*, *Cryptococcus neoformans*, etc. Essentially, applicants recite the claimed sequences by the property of their not being present in *C. albicans* or *S. cerevisiae* or, alternatively, being present in a extensive list of microorganisms without disclosing the structures of any sequences thereof or any

properties of the proteins encoded by the claimed sequences. It must be considered that the skilled artisan would conclude that applicants' disclosure of SEQ ID NO:6068 would not be a representative number of species sufficient to describe the claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-33 and 35-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 is vague in the recitation of the phrases "A purified or isolated nucleic acid molecule **comprises** (emphasis added) a nucleotide..." and "...said gene product **consisting** (emphasis added) essentially of..." as the language of the transitional phrases does not agree with the nouns. Redrafting the claim to recite "A purified or isolated nucleic acid molecule comprising a nucleotide..." and "...said gene product consists essentially of..." would be remedial.

Claim 35 is vague in the recitation of the phrase "...hybridizes under stringent **condition** (emphasis added) to a second nucleic acid..." because "condition" should be plural (conditions). Also, in line 6 of the claim "condition" should also be plural (conditions).

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0767. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo
July 28, 2004

DAVID GUZO
PRIMARY EXAMINER